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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/656,192	09/08/2003	Mark J. Cooper	003659.00029	8424
22907 7590 01/15/2008 BANNER & WITCOFF, LTD. 1100 13th STREET, N.W. SUITE 1200 WASHINGTON, DC 20005-4051			EXAMINER LONG, SCOTT	
			ART UNIT 1633	PAPER NUMBER
			MAIL DATE 01/15/2008	DELIVERY MODE PAPER

**Please find below and/or attached an Office communication concerning this application or proceeding.**

The time period for reply, if any, is set in the attached communication.

## Office Action Summary

### Application No.

10/656,192

### Applicant(s)

COOPER ET AL.

### Examiner

Scott D. Long

### Art Unit

1633

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

### Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

### Status

- 1) ☒ Responsive to communication(s) filed on 06 November 2007.
- 2a) ☐ This action is **FINAL**. 2b) ☒ This action is non-final.
- 3) ☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

### Disposition of Claims

- 4) ☒ Claim(s) See Continuation Sheet is/are pending in the application.
- 4a) Of the above claim(s) \_\_\_\_\_ is/are withdrawn from consideration.
- 5) ☐ Claim(s) \_\_\_\_\_ is/are allowed.
- 6) ☒ Claim(s) 1-5, 8-14, 17-19, 26, 28, 30-31, 34-35, 38-40, 51-55, 58-70, 73-82, 103-104, 106-107, 114-115, and 122 is/are rejected.
- 7) ☐ Claim(s) \_\_\_\_\_ is/are objected to.
- 8) ☐ Claim(s) \_\_\_\_\_ are subject to restriction and/or election requirement.

### Application Papers

- 9) ☐ The specification is objected to by the Examiner.
- 10) ☐ The drawing(s) filed on \_\_\_\_\_ is/are: a) ☐ accepted or b) ☐ objected to by the Examiner.  
Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).  
Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).
- 11) ☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

### Priority under 35 U.S.C. § 119

- 12) ☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).
- a) ☐ All b) ☐ Some \* c) ☐ None of:
1. ☐ Certified copies of the priority documents have been received.
  2. ☐ Certified copies of the priority documents have been received in Application No. \_\_\_\_\_.
  3. ☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).
- \* See the attached detailed Office action for a list of the certified copies not received.

### Attachment(s)

- 1) ☒ Notice of References Cited (PTO-892)
- 2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
- 3) ☒ Information Disclosure Statement(s) (PTO/SB/08)  
Paper No(s)/Mail Date 11/2007.
- 4) ☐ Interview Summary (PTO-413)  
Paper No(s)/Mail Date. \_\_\_\_\_
- 5) ☐ Notice of Informal Patent Application
- 6) ☐ Other: \_\_\_\_\_

Continuation of Disposition of Claims: Claims pending in the application are 1-5,8-14,17-19,26,28,30,31,34,35,38-40,51-55,58-70,73-82,103,104,106,107,114,115 and 122.

## **DETAILED ACTION**

### ***Continued Examination Under 37 CFR 1.114***

A request for continued examination under 37 CFR 1.114, including the fee set forth in 37 CFR 1.17(e), was filed in this application after final rejection. Since this application is eligible for continued examination under 37 CFR 1.114, and the fee set forth in 37 CFR 1.17(e) has been timely paid, the finality of the previous Office action has been withdrawn pursuant to 37 CFR 1.114. Applicant's submission filed on 11/6/2007 has been entered.

### ***Claim Status***

Claims 1, 8, 17, 26, and 28 are amended. Claims 6-7, 15-16, 20-25, 27, 29, 32-33, 36-37, 41-50, 56-57, 71-72, 83-102, 105, 108-113, 116-121, and 123 are cancelled. Claims 1-5, 8-14, 17-19, 26, 28, 30-31, 34-35, 38-40, 51-55, 58-70, 73-82, 103-104, 106-107, 114-115, and 122 are under current examination.

### ***Priority***

This application claims benefit from U.S. Application No. 2002/0042388 (abandoned), filed 31 May 2001, provisional U.S. provisional Application No. 60/287,419, filed 31 May 2001, and U.S. provisional Application No. 60/207,949, filed 31 May 2000. The instant application has been granted the benefit date, 31 May 2000, from the application 60/207,949. However, the examiner notes that the provisional application makes no mention of lyophilization or disaccharides.

**37 CFR 1.132 Affidavit**

The affidavit under 37 CFR 1.132 filed 11/6/2007 is sufficient to overcome the rejection of claims 1-5, 8-14, 17-19, 26, 28, 30-31, 34-35, 38-40, 51-55, 58-70, 73-82, 103-104, 106-107, 114-115, and 122 under 35 USC 112, 1<sup>st</sup> paragraph, based on the lack of enablement for gene therapy methods. See Response to Arguments, 35 USC 112, 1<sup>st</sup> paragraph (lack of enablement) section for full discussion.

***Response to Arguments - Claim Rejections 35 USC § 112***

Applicant's arguments (Remarks, pages 11-12, filed 11/6/2007) and claim amendments, regarding rejection of claims 1-5, 8-14, 17-19, 26, 28, 30-31, 34-35, 38-40, 51-55, 58-70, 73-82, 103-104, 106-107, 114-115, and 122 have been fully considered and they are partially persuasive.

The applicant's claim amendments of claims 1, 8, 17, 26, and 28 have altered the scope of the claims such that the claimed composition inherently comprises more than merely rod-shaped complexes. Therefore, the rejection of the instant claims based on lack of enablement on making complexes that are solely rod-shaped is overcome by the claim amendments. Therefore, the examiner withdraws this portion of the 35 USC 112, 1<sup>st</sup> paragraph rejection.

The applicants have submitted an affidavit under Rule 132 by Dr. Mark J. Cooper, co-applicant of the instant application and co-author of Konstan et al. (Human

Gene Therapy, 2004, 15:1255-1269). In the affidavit, Dr. Cooper has affirmed that the instantly claimed compositions are the same as those used in the Konstan et al. reference, in which at least a minimal level of CFTR gene was expressed after intranasal administration of said compositions comprising condensed rod-shaped complexes. The examiner accepts this affirmation as sufficient to overcome the lack of enablement rejection of claims 1-5, 8-14, 17-19, 26, 28, 30-31, 34-35, 38-40, 51-55, 58-70, 73-82, 103-104, 106-107, 114-115, and 122 based on the lack of enablement for gene therapy methods. The scope of the instant claims directed to methods is limited to methods of delivery, uptake, and expression of genes. The claimed methods do not specifically claim methods of therapy or treatment. Therefore, in light of the Cooper Affidavit, the examiner believes the instant claims are fully enabled. Therefore, the examiner withdraws this portion of the 35 USC 112, 1<sup>st</sup> paragraph rejection.

Therefore, the examiner hereby withdraws the rejection of claims of 1-5, 8-14, 17-19, 26, 28, 30-31, 34-35, 38-40, 51-55, 58-70, 73-82, 103-104, 106-107, 114-115, and 122 under 35 USC 112, 1<sup>st</sup> paragraph rejection (lack of enablement).

***Response to Amendments - Claim Rejections 35 USC § 102 and § 103***

Applicant's arguments (Remarks, pages 14-17, filed 11/6/2007) and claim amendments, regarding rejection of claims 1-5, 8-14, 17-19, 26, 28, 30-31, 34-35, 38-40, 51-55, 58-70, 73-82, 103-104, 106-107, 114-115, and 122 under 35 USC 102 and 103 have been fully considered but they are unpersuasive.

Fundamentally, the applicant's arguments (Remarks, pages 14-17) against all of the prior art rejections under 35 USC 102 and 103 rest on whether the rod-like structures taught by Hanson (US 5,844,107) in fact meet the limitations of the instant claims.

The applicant presents several teachings of Hanson which describe the nature of relaxed and condensed DNA. The applicant also cites Hanson's discussion of relaxed DNA as forming fibers (Remarks, middle of page 14). The applicant also insightfully cites Hanson's description of Figure 1F, wherein Hanson describes a salt concentration "above optimal for condensation" and wherein "[t]he DNA is in a relaxed state...and the rod-like DNA fibers" (Remarks, bottom of page 14, and Hanson col.6, lines 11-16). The examiner completely agrees with the applicant's presentation of Hanson's teachings up to this point in his argument.

However, the examiner does not agree with the applicant's conclusion, "[t]he only rod-like structures Hanson teaches are fiber-containing complexes which are not condensed as required by the claims....Hanson therefore does not teach the formation of rod-shaped complexes of condensed nucleic acid" (Remarks, bottom of page 14 to top of page 15). Hanson teaches "electron microscopic results have been indicated as follows:...the structure resulting from condensation are rod-like relaxed toroids of increased size" (col.62, lines 51-57). This teaching is remarkably similar to that of the instant application, "DNA condensed with acetate and bicarbonate salts of CK30 polylysine assumed forms of long (100-300 nm) and narrow (10-20 nm) rods and relaxed toroids (~50-100 nm diameter, 10-20 nm width)" (specification, page 16, lines 1-

3). Since Hanson teaches compositions comprising condensed DNA/polylysine cation/acetate counterion complexes and at least a subset of these complexes are rod-shaped as visualized by electron microscopy and Hanson further teaches that the shape of these condensed complexes is due in part to the salt concentrations, the examiner believes that the rod-like, relaxed toroids of Hanson satisfy the claim limitations of the instant application.

Regarding the assertion that the "rod-like fibers" described in Figure 1F, the examiner believes that these are in fact the same "rod-like relaxed toroids" described above. Hanson teaches, "[r]od-like fibers (usually 10-20 times the diameter of a naked DNA fiber, i.e., usually 10-20 nm thick and longer than 60 nm) of DNA and branched toroidal structures of increased size (FIG. 1F)" (Table 103, col. 57-58, Electron Microscopy section). In this quotation, the "rod-like fibers" are not referring to DNA fibers associated with precipitated, aggregated DNA, because Hanson contrasts the rod-like fibers with naked DNA fibers. It is clear that these two "fibers" are not the same. Furthermore, the size of the "rod-like fibers" is in the same range as that taught by the applicant for his relaxed toroids (~50-100 nm diameter, 10-20 nm width). The examiner believes the "rod-like fibers" of Hanson's Figure F1 are the same as the applicant's "relaxed toroids". A relaxed toroid structure is not the same as relaxed DNA. In fact, Hanson describes relaxed DNA as "non-complexed" and contrasts this with "condensed form" (col. 8, line 67). A PLL-DNA composition having relaxed-toroid form is complexed and condensed.



Taken as a whole, neither Hanson nor the instant specification devote much time or many words to the “rod-shaped” structures so strenuously argued by the applicant. As is clear from Hanson, and as is well understood in the art, the process of condensing nucleic acids with polycations (e.g., PLL) and counterions (e.g., acetate), can produce condensed nucleic acid complexes having a variety of shapes including spheres, toroids, relaxed toroids (sometime called rods), and branched toroidal (Y-shaped) structures (page 182 of Kwoh et al. (Biochim Biophys. 1444 (1999) 171-190) shows beautiful photos demonstrating the extreme heterogeneity of DNA/PLL complexes). The examiner believes the claims of the instant application to be obvious over the prior art. As described in previous actions and above, the examiner also believes Hanson teaches the base claims and some other claims. The remaining dependent claims augment the teachings of Hanson to satisfy the many obvious claim limitations also taught by other researchers in the art. Furthermore, the field has been performing routine optimization using these compounds for years, varying all the usual factors (salt, cation type and length, etc.) known to be important for compaction. The applicant has not claimed anything more than what has been known in the art. Furthermore, the intense focus in the applicant’s arguments on a particular subset (rod-shaped) of the variety of compacted forms of DNA-PLL complexes commonly produced by known methods has not been explained in the specification. Therefore, the examiner cannot find the compositions of the instant claims to be unobvious variants of what has been performed by others skilled in the art.

Therefore, the rejection of the instant claims as anticipated by Hanson and as obvious over Hanson and others (see Action, filed 6/6/2007), is hereby maintained for the reasons of record and the comments above.

***Response to Argument – Double Patenting***

The applicant correctly points out that the examiner erroneously rejected the instant claims under nonstatutory double-patenting. The two applications (10/307555 and 10/307284) against which the examiner applied ODP rejections were, in fact, divisionals from the parent application (09/867693) of the instant application. The instant application is a Continuation of 09/867693. Therefore, the examiner hereby withdraws both ODP rejections of the instant claims.

***Conclusion***

No claims are allowed.

***Examiner Contact Information***

Any inquiry concerning this communication or earlier communications from the examiner should be directed to **Scott Long** whose telephone number is **571-272-9048**. The examiner can normally be reached on Monday - Friday, 9am - 5pm.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, **Joseph Woitach** can be reached on **571-272-0739**. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see <http://pair-direct.uspto.gov>. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free).

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